

## **DETAILED ACTION**

Applicant's amendments filed 15 February 2008 are acknowledged and entered.

### ***Status of Claims***

Cancellation of claims 45-55, 57, 58 and 71 are acknowledged. Addition of new claim 72 is acknowledged. Claims 60, 62-70 and 72 are currently pending and under consideration.

### ***Withdrawn Rejections/Objections***

The rejection of claims 45-50, 52-55, 57 and 58 under 35 U.S.C. 103(a) over Handique in view of Wilding and in view of Ramsey, in the Office action mailed 18 October 2007 is withdrawn in view of the amendment filed 15 February 2008.

The rejection of claim 51 under 35 U.S.C. 103(a) over Handique in view of Wilding in view of Ramsey and further in view of Burns, in the Office action mailed 18 October 2007 is withdrawn in view of the amendment filed 15 February 2008.

The rejection of claim 71 under 35 U.S.C. 103(a) over Handique in view of Wilding further in view of Manz, in the Office action mailed 18 October 2007 is withdrawn in view of the amendment filed 15 February 2008.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 60 and 62-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Handique et al. in view of Wilding et al.

The instant claims are drawn to an apparatus and method for analyzing a sample comprising a body, reaction chamber, separation region, transition region connecting said chamber and channel that is thermally isolated, optically monitoring said reaction chamber for reaction product, a valve in said transition region, opening said valve in said transition region, injecting a plug of reaction product into separation region, detecting said reaction product and electrodes coupled to said body.

The abstract of Handique et al. discloses the central invention as being directed to the movement and mixing of microdroplets through microchannels in devices with reaction chambers, electrophoresis modules, etc. These elements are also summarized in column 3, line 49, through column 4, line 32, which includes various reaction and analysis practices. The use of electrodes positioned in a channel so as to move liquid when a potential is applied is disclosed in column 7, line 53, through column 8, line 44, which also described flow constricting means in such channels. Various other flow constricting elements are present in the channels as noted in column 10, lines 57-65. In column 13, lines 19-34, a device of the invention includes reaction chamber, channels which serve as transition regions connecting said chamber, and an electrophoresis modules which is a separation region where migration data is detected regarding electrophoretic separation. Such a separation via electrophoresis is further detailed in column 21, lines 35-67, including optics for detecting bands from said electrophoresis separation region. These devices are microfabricated with the regions etc. therein reasonably interpreted as enclosed as described in column 3, line 65, through column 4, line 10, in an integrated system. Thermal conduction is limited in the device so that droplet movement can be controlled as noted in column 8, lines 1-9, via differential heating. The practice of a two part device with electrical pads as needed in a second or appliance type of element is disclosed in column 13, lines 49-59. The presence of heaters in the substrate are also described in a two part device as noted in column 18, line 40, through column 19, line 44. Side channels with flow control may also be utilized

in the device of the invention as disclosed in column 14, line 24, through column 15, line 19.

Handique et al. as applied to 60 and 62-70, does not optically monitor the reaction chamber for product.

Wilding et al. also describes devices and production thereof for microscale reaction~analysis practice and has previously been cited in the prosecution history of this application as citing reaction chamber, transition region, and separation region elements for such devices and therefore is of the same subject matter type as the above noted Handique et al. invention. In Wilding et al. in column 7, lines 22-38, microfabrication of devices of this microscale or mesoscale type is suggested and motivated to be equivalently usable when made by silicon photolithography wherein the silicon may be polysilicon, polyimide, etc. as well as produced via plastic molding. Thus, a reasonable expectation of success in producing such devices and thus describing the devices per se is set forth for polymeric molding of devices of this type. Wilding et al. also includes optical monitoring of reaction product before entering into the separation region, in column 19, lines 31-37.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to produce or practice the electrode/voltage invention of Handique et al. with various microfabricated polymeric materials as equivalent as described in Wilding et al. to result in a reasonable expectation of success to practice the device and/or combination of device with appliance substrate of the instant invention or production thereof.

Claim 72 is rejected under 35 U.S.C. 103(a) as being unpatentable over Handique et al. in view of Wilding et al. as applied to claims 60 and 62-70 above, and further in view of Manz et al.

The instant claims are drawn to an apparatus and method for analyzing a sample comprising a body, reaction chamber, separation region, transition region connecting said chamber and channel that is thermally isolated, optically monitoring said reaction chamber for reaction product, a valve in said transition region, opening said valve in said transition region, injecting a plug of reaction product into separation region, detecting said reaction product and electrodes coupled to said body, wherein the reaction product are separated by isoelectric focusing.

Handique et al. in view of Wilding et al. as applied to claims 60 and 62-70 above, do not show separating product by isoelectric focusing.

Manz et al. provide a device and method for the electrophoretic separation of fluid substance mixtures. Manz shows separation of product by isoelectric focusing in the first phase of separation, see column 5, lines 28-38.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to produce or practice the electrode/voltage invention of Handique et al. with various microfabricated polymeric materials as equivalent as described in Wilding et al. and separating product with isoelectric focusing as described in Manz et al. to result in a reasonable expectation of success to practice the device and/or

combination of device with appliance substrate of the instant invention or production thereof.

***Response to Arguments***

Applicants' arguments filed 15 February 2008 have been fully considered but they are not persuasive.

Applicants argue that Handique et al. and Wilding et al. do not teach nor suggest having a valve as presently claimed in independent claim 60. Handique et al. showing of a valve in a side channel does not suggest applicant's method. Handique teaches away from using valves in the device of Figure 1 and quotes that the Handique invention does not require the use of valves.

Applicants argue that the references do not teach nor suggest the steps of subjecting the sample to a reaction while the valve is closed as recited in step (b) of claim 60, nor teach opening the valve before injection a sample plug into the separation region as recited in steps (e) and (f) of claim 60.

Applicants argue that Wilding does not teach nor suggest the use of optically monitoring the reaction chamber for reaction product. Specifically that Wilding does not teach or suggest optically monitoring the reaction chamber and determining if sufficient reaction products have been generated prior to injecting the sample plug into the separation region and then separating and detecting the reaction products as recited in claim 60.

Applicants argue that the invention's use of a valve between the reaction chamber and the separation channel, overcomes problems such as bubbles, produced

from the reactions or with pressure, combined with elevated temperature. Applicants' argue that the argument above apply to dependent claims 62-70 and 72.

Applicants' arguments have been fully considered but they are not persuasive.

As recited in the Board of Patent Appeals and Interferences, *Ex parte M. Allen Northrop, Kurt E. Peterson, William A. McMillan, and Gregory T.A. Kovacs*, on 28 June 2007:

"Appellants' contend that the cited prior art fails to teach or suggest a valve to control fluid between the reaction and separation regions as required by claims 45 and 60 (Br. 4). They assert that high pressures can develop in reaction chambers due to gas expansion (Br. 4). They state that this pressure "can have detrimental effects on the separation medium (e.g., gel) in the separation channel" and cause chemicals to flow or diffuse into the separation region (Br. 4). Appellants' assert that the device of claim 45 overcomes "these problems with at least one valve in a transition region between the reaction chamber and separation region" (Br. 4). Appellants argue that "Handique teaches away from placing valves in the device of Fig. 1" (Br. 4) because Handique explicitly states that its invention "contemplates the use of selective hydrophobic coatings to develop a liquid-sample injection and motion system that does not require the use of valves" (Handique, col. 13, 11.63-66).

Obviousness requires a teaching that all elements of the claimed invention are found in the prior art and "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007). We agree with the Examiner that the cited prior art provides adequate reason to have placed a valve "in the transition region" for controlling fluid flow between the reaction chamber and the separation channel as required by claims 45 and 60.

As established by the Examiner (Answer 3, 7), Handique teaches that its device comprises "sealed valves to control fluid flow" (Handique, col. 16, 11.40-43; Findings of Fact 5). Handique describes several types of valves (Findings of Fact 6-8). While Handique does not explicitly teach a valve between its reaction chamber (C) and electrophoresis module (D), the skilled worker would have recognized the advantage in placing a valve at this junction. Handique teaches that "mixing and reactions" occur in the reaction chamber prior to entry in the electrophoresis module (D) (Handique, col. 13, 11. 19-30; Findings of Fact 2, 11). In Example 5, which involved testing the device components for biocompatibility, the "reaction mix [was] covered with mineral oil to prevent evaporation" (Handique, col. 28, 11.27-30; Findings of Fact 12). The reaction is described to occur in a "containment chamber" (Handique, col 28, 11.35-36; Findings of Fact 13). Nucleic acid amplification reaction involves several temperature and enzyme cycling steps (Handique, col. 28, 11.30-33; Findings of Fact 14). Thus, the skilled

worker would have recognized the advantage of placing a valve between chamber (C) and electrophoresis module (D) to contain the reaction and to prevent evaporation during the long reaction time.

Furthermore, Wilding explicitly teaches sealing the reaction chamber which "advantageously prevents evaporation of liquids during thermal recycling and thus maintains the preferred reaction concentrations during the amplification reaction" (Wilding, col. 7, 11. 57-62). See Findings of Fact 18- 19; Answer 7. Wilding's teaching provides a reason to have placed a valve between the reaction chamber and separation channel: to prevent evaporation during thermal recycling, thus making the claimed invention obvious over Handique in view of Wilding.

Appellants' argue that "Handique teaches away from placing valves in the device of Fig. 1" (Br. 4) because Handique explicitly states that its invention "contemplates the use of selective hydrophobic coatings to develop a liquid-sample injection and motion system that does not require the use of valves" (Handique, col. 13, 11. 63-66). We are not convinced by this argument. As stated by the Examiner, "a reference is relied upon for the totality of its teachings" (Answer 7). See *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1550-51,220 USPQ 303,311 (Fed. Cir. 1983) (the totality of a reference's teachings must be considered), cert. denied, 469 U.S. 851 (1984); *In re Gurley*, 27 F.3d 551,553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Handique contains numerous references to valves, including the statement that its device "contemplates the use of sealed valves to control fluid flow" (Handique, col. 16, 11.40-42; Findings of Fact 5. See also Handique, col. 8, 11.23-39; col. 16, 11.43-61; col. 30, 11.5-15; Fig. 12; Findings of Fact 6-9). Handique also describes manufacturing a sealable valve (Handique, col. 12, 11. 3-4; Fig. 12; Findings of Fact 9). Thus, contrary to Appellants' assertions, Handique discloses the use of valves in its device. Handique's statement that valves are not "required" for its "a liquid-sample injection and motion system" (Handique, col. 13, 11.63-66) clearly does not mean that valves cannot be part of its device since valves are explicitly disclosed in certain embodiments of Handique. Appellants' also state that "[w]here Handique shows a valve is in the different device of Fig. 13" (Br. 5). We do not find this argument persuasive. According to Handique, "Fig. 13 is a schematic of one embodiment for the layout of the movable sealing means of the present invention" (Handique, col. 12, 11.5-6). Thus, Fig. 13 is not stated by Handique to show a complete device; it is an illustration of a valve that can be utilized in its device. With regard to Wilding, Appellants' state that the reference "fails to teach or suggest a device having a valve in a transition region that connects a reaction chamber to a separation channel" (Br. 8). We do not find this argument persuasive. Wilding explicitly states that its device can contain a reversibly sealable port to contain fluid in the reaction chamber and prevent evaporation (Wilding, col. 7, 11. 57-66; Findings of Fact 19-20), providing a reason to have placed a sealing valve in the transition region of Handique's device.

#### Obviousness of claims 60 and 62-70

Claim 60 is directed to a "method for analyzing a sample" using a device which comprises a reaction chamber, separation channel, transition region, at least one valve

in the transition region. In step d), claim 60 requires "injecting into the separation region a sample plug containing reaction products."

The Examiner contends that "[i]t would further have been obvious to have injected a sample as a 'plug' [as required by claim 60] in the method of [Handique] where the motivation would have been to improve electrophoretic resolution, as taught by [Handique] as being a desired result (col. 21, lines 37-51)" (Answer 5). As we agree with this reasoning, and since Appellants' do not identify any defect in it, we affirm the rejection of claim 60. Because separate reasons for their patentability were not provided, claims 62-70 fall with claim 60.

Wilding et al. shows an optical system that allows monitoring of contents for changes in fluid properties, such as low properties or color, induced by the presence of polynucleotide amplification product and addition or removal of fluid samples to and from reaction chambers may be monitored optically, (column 19, lines 16-37).

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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